At page 15, line 3, delete "(right panels)" and substitute therefor --3A-1 through 3E-1, respectively--.

In the Claims:

Please amend claims 43-46, 68-79, and 89-92 and add new claims 94-100 as indicated.

43. (Amended) A method for specifically cleaving a preselected RNA comprising contacting said RNA with an oligomeric compound comprising at least twelve ribofuranosyl [nucleosides] nucleoside subunits in a sequence which is specifically hybridizable with said preselected RNA;

said nucleoside subunits being joined by internucleoside bonds which are more stable to degradation as compared to phosphodiester bonds;

the compound having [at least one segment comprising] at least one modified nucleoside subunit, which modified nucleoside subunit is modified to improve at least one of: pharmacokinetic binding, absorption, distribution or clearance properties of the compound; affinity or specificity of said compound to said target RNA; or modification of the charge of said compound as compared to an unmodified compound; and

said compound having [a further segment having] at least four consecutive 2'-hydroxyl ribonucleoside subunits.

B1

44. (Amended) The method of claim 43 wherein said [further segment] compound has at least five consecutive ribonucleoside subunits.

45. (Amended) A method for treating an organism having a disease [characterized by the undesired production of a protein] comprising contacting the organism with an oligomeric compound [of the invention] having a sequence of nucleoside subunits capable of specifically hybridizing with a complementary strand of ribonucleic acid with at least one of the nucleoside subunits being modified to improve at least one of: pharmacokinetic binding, absorption, distribution or clearance properties of the compound; affinity or specificity of said compound to said target RNA; or

modification of the charge of said compound as compared to unmodified compound; and a plurality of the nucleoside subunits being located in a consecutive sequence and having 2'-hydroxyl-pentofuranosyl sugar moieties.

B1 cont.

46. (Amended) A [compositions] composition including a pharmaceutically effective amount of an oligomeric compound in a pharmaceutically acceptable diluent or carrier, said oligomeric compound comprising a sequence of nucleoside subunits capable of specifically hybridizing with a complementary strand of RNA wherein a plurality of the nucleoside subunits of the oligomeric compound are modified to improve at least one of: pharmacokinetic binding, absorption, distribution or clearance properties of the compound; affinity or specificity of said compound to said target RNA; or modification of the charge of said compound as compared to an unmodified compound; and wherein a further plurality of the nucleoside subunits have 2'-hydroxyl-pentofuranosyl sugar moieties.

B2

68. (Amended) A mammalian ribonuclease having the activity of catalyzing the degradation of a double stranded substrate wherein one of said strands of said substrate is a [mRNA] RNA and the other of said strands of said substrate comprises a compound having [in sequence a first segment comprising] a plurality of 2' modified nucleoside subunits and [a second segment comprising] at least four consecutive ribofuranosyl nucleoside subunits having 2'-hydroxyl moieties thereon.

69. (Amended) A mammalian ribonuclease of claim 68 wherein said subunits [of said compound] are joined by phosphorothioate internucleoside linkages or phosphodiester internucleoside linkages.

70. (Amended) A mammalian ribonuclease of claim 68 wherein a portion of said subunits [of said first segment of said compound] are joined by phosphorothioate internucleoside linkages.

71. (Amended) A mammalian ribonuclease of claim 70 wherein said subunits [of said second segment of said compound] are joined by phosphodiester internucleoside linkages.

72. (Amended) A mammalian ribonuclease of claim 70 wherein all of said subunits [of said second segment of said compound] are joined by phosphorothioate internucleoside linkages.

73. (Amended) A mammalian ribonuclease of claim 68 wherein at least some of said subunits [of said first segment of said compound] are 2'-O-alkyl nucleoside subunits.

74. (Amended) A mammalian ribonuclease [of claim 68,] having the activity of catalyzing the degradation of a double stranded substrate wherein:

[(A)] said activity is inhibited by NaCl;

[(B)] said activity requires Mg++; and

[(D)] said mammalian ribonuclease has an apaprent molecular weight, as determined by SDS-PAGE, of about 50 to about 80 kilodaltons.

75. (Amended) A mammalian ribonuclease of claim [68] 74, wherein said ribonuclease is isolated from nucleii.

B2 cont

76. (Amended) A mammalian ribonuclease of claim [68] 74, wherein said ribonuclease is isolated from cytosol.

77. (Amended) The mammalian [protein] ribonuclease of claim [68] 74, wherein said ribonuclease is isolatable from human cells or tissues.

78. (Amended) A double-stranded RNA substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein

[(A)] said first and said second oligonucleotide each have a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each [other] other in said duplex;

[(B)] at least one of said first and said second oligonucleotides have portions flanking said central portions having chemical modifications which make them resistant to single-stranded nucleases.

79. (Amended) A double-stranded RNA substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein

B2 Cont

[(A)] said first and said second oligonucleotide each have a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each [other] other in said duplex;

[(B)] at least one of said first and said second oligonucleotides have portions flanking said central portions having chemical modifications which make them resistant to single-stranded nucleases and increase their affinity for the [other] other oligonucleotide of the duplex.

89. (Amended) Use of said ribonuclease of claim [68] 74 for treating an organism having a disease characterized by the undesired production of a protein encoded by [said mRMA] a mRNA.

SUB E1

90. (Amended) Use of said ribonuclease of claim [68] 74 for identifying one of [said] a mRNA or a protein encoded by said mRNA.

B3

SUB E2

91. (Amended) Use of said ribonuclease of claim [68] 74 for diagnosing an aberrant state in an organism associated with a protein encoded by [said] a mRNA.

92. (Amended) A mammalian ribonuclease having the activity of catalyzing the degradation of a double stranded substrate wherein one of said strands of said substrate is a [mRNA] RNA and

B3 Cont.

at least one of said first and second oligonucleotides include a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases and that increases the affinity for said oligonucleotide for the other of said oligonucleotides.

98. A double-stranded RNA comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein at least one of said first and said second oligonucleotides includes a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases and that increases the affinity for said oligonucleotide for the other of said oligonucleotides.

95

99. A double-stranded RNA comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein at least one of said first and said second oligonucleotides includes a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases.

B4

96

100. A double-stranded RNA comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein at least one of said first and said second oligonucleotides includes a chemical modification that increases the affinity for said oligonucleotide for the other of said oligonucleotides.--

REMARKS

Claims 43-46, 68-82, and 89-93 are pending in the present application. Claims 43-46, 68-79, and 89-92 have been amended herein. New claims 94-100 have been added. Upon entry of the present Preliminary Amendment, claims 43-46, 68-82, and 89-100 will be pending.

The specification has been amended to comport with the Figure nomenclature for the formal drawings.